**Supplementary Table 1**. Comparison of BLISS with other methods for genome-wide DSB detection.

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| --- | --- | --- | --- | --- |
| **Method** | **Detection** | **Main features** | **Sample (input)** | **Reported applications** |
| BLISS | Direct | *In situ* DSB blunting and ligation in cells and tissue sections attached onto a solid surface. Selective amplification of DSB ends by *in vitro* transcription. Quantitative power thanks to UMIs. | Fixed cells, tissue sections (compatibility with low-input samples of 103 cells) | Etoposide-induced DSBs. Natural DSBs in cells and tissues. Cas9 and Cpf1 specificity (this paper) |
| BLESS | Direct | *In situ* DSB blunting and ligation of biotinylated adapters. DSB capture on streptavidin | Fixed cells  (at least 106 cells) | Replication stress-induced DSBs in mammalian cells[(Crosetto et al. 2013)](https://paperpile.com/c/Khgo8j/8Prqo), Cas9 specificity [(Ran et al. 2015)](https://paperpile.com/c/Khgo8j/Nfxb0)[(Slaymaker et al. 2016)https://paperpile.com/c/Khgo8j/SGS3L](https://paperpile.com/c/Khgo8j/SGS3L) |
| DSBCapture | Direct | *In situ* DSB blunting and A-tailing. Modified BLESS adapters containing Illumina adapter sequences | Fixed cells  (at least 106 cells) | DSBs at G-quadruplex rich sites, active genes and transcription start sites [(Lensing et al. 2016)https://paperpile.com/c/Khgo8j/R7DBE](https://paperpile.com/c/Khgo8j/R7DBE) |
| End-Seq | Direct | *In vivo* DSB blunting and A-tailing in agarose plugs. Modified BLESS adapters containing Illumina adapter sequences | Live cells  (at least 107 cells) | AsiSI-induced DSBs resection mapping, RAG endonuclease specificity [(Canela et al. 2016)https://paperpile.com/c/Khgo8j/Cc4Rk](https://paperpile.com/c/Khgo8j/Cc4Rk) |
| Digenome-seq | Direct | *In vitro* nucleasedigestion of purified genomic DNA and detection of DSBs by whole-genome sequencing | Purified DNA | Cas9 and Cpf1 specificity [(Kim et al. 2016; Kim et al. 2015)https://paperpile.com/c/Khgo8j/pT1qb+d4hZg](https://paperpile.com/c/Khgo8j/pT1qb+d4hZg) |
| ChIP-seq | Indirect | Capture of chromatin containing DSBs markers such as γH2A.X | Fixed cells  (at least 107 cells) | Replication stress-induced DSBs in yeast [(Szilard et al. 2010)](https://paperpile.com/c/Khgo8j/tEcZG), AsiSI-induced DSBs processing in mammalian cells [(Iacovoni et al. 2010)](https://paperpile.com/c/Khgo8j/6PXaa), transcription-associated DSBs in neuronal cells [(Madabhushi et al. 2015)https://paperpile.com/c/Khgo8j/gHd5K](https://paperpile.com/c/Khgo8j/gHd5K) |
| GUIDE-seq | Indirect | *In vivo* DSB labeling by incorporation of dsDNA oligos through NHEJ-mediated repair | Transfected live cells | Cas9 and Cpf1 specificity [(Tsai et al. 2015)](https://paperpile.com/c/Khgo8j/iWJVm)[(Kleinstiver et al. 2016)https://paperpile.com/c/Khgo8j/M0f7U](https://paperpile.com/c/Khgo8j/M0f7U) |
| IDLV capture | Indirect | *In vivo* DSB labeling by random incorporation of integration defective lentiviral vectors through NHEJ-mediated repair | Transduced live cells | Cas9 and TALENs specificity [(Wang et al. 2015)https://paperpile.com/c/Khgo8j/XGIcf](https://paperpile.com/c/Khgo8j/XGIcf) |
| LAM-HTGTS | Indirect | *In vivo* induction of DSBs and sequencing of translocation products originated from NHEJ-mediated repair | Live cells treated to induce translocations | Cas9 specificity [(Frock et al. 2015)](https://paperpile.com/c/Khgo8j/Cxxsn), transcription-associated DSBs in neuronal cells [(Wei et al. 2016)https://paperpile.com/c/Khgo8j/AS8ja](https://paperpile.com/c/Khgo8j/AS8ja) |